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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,784	LI ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-44* is/are pending in the application.

4a) Of the above claim(s) *40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-39, and 43-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 37-44 are pending.

2. Claims 40-42 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a non-elected invention.

3. Claims 37-39, and 43-44, drawn to an antibody or binding fragment thereof specifically binds to SEQ ID NO: 2, are being acted upon in this Office Action.

4. In view of the amendment filed 6/25/07, the following rejections remain.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 43-44 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 recites the limitation "a heteroconjugate". There is insufficient antecedent basis for this limitation in the claim. This is because the antibody in base claim 37 is unconjugated and suddenly the antibody in claim 43 becomes heteroconjugated antibody. It is suggested that claim 43 be amended to recite "A heteroconjugated antibody wherein the antibody is the antibody of claim 37."

Claim 44 recites the limitation "bispecific antibody". It is not clear as the binding specificity of the other arm since the antibody is bispecific. One of ordinary skilled in the art cannot appraise the metes and bound of the claimed invention.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 37-38 and 44 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO98/30582 publication (of record, July 16, 1998; PTO 892).

The WO 98/30582 publication, of record, teaches a protein such as AAV40509 that is 92.9% identical to the claimed SEQ ID NO: 2 and antibody that binds to the reference protein (see enclosed sequence alignment, page 56, lines 33-34, in particular). The WO 98/30582 publication further teaches an antibody such as a monoclonal antibody that binds to another protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). Given the long stretch of identical amino acids to which the reference antibody binds, the reference antibody inherently also binds to the claimed polypeptide of SEQ ID NO: 2. Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Claim 44 is included in this rejection because the WO98/30582 publication also teaches a label conjugated antibody (heteroconjugate antibody) for detection assays (see page 35, line 32-34, page 56, lines 33-34, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 6/25/07 have been fully considered but are not found persuasive.

Applicants' position is that claim 37 has been amended and the WO98/30582 does not teach antibodies that specifically bind to amino acid residues 105-187.

In response, the WO 98/30582 publication teaches an antibody such as a monoclonal antibody that binds to a protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). The reference antibody made using the reference protein obviously cross-reacts with the claimed SEQ ID NO: 2.

Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/30582 publication (of record, July 16, 1998; PTO 892) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 626-629; PTO 892).

The teachings of the WO98/30582 publication have been discussed supra. The WO 98/30582 publication further teaches the reference antibody is useful for diagnostic reagents and therapeutics for condition such as cancer associated with the reference protein (see page 57, lines 1-2, in particular).

The invention in claim 37 differs from the teachings of the reference only in that the antibody specifically for SEQ ID NO: 2 is a binding fragment instead of a whole antibody.

Harlow *et al* further teach a method of producing antibody fragment such as Fab or $F(ab')_2$ fragment (See page 626-629, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce antibody fragment as taught by Harlow *et al* with the antibody that bind to EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166

amino acid residues identical to the claimed SEQ ID NO: 2 or the antibody that binds AAV40509 that is 92.9% identical to the claimed SEQ ID NO: 2 as taught by WO98/30582 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to make antibody fragment because Harlow *et al* teach that the advantage of using antibody fragment can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626, in particular). The WO 98/30582 publication teaches the reference antibody is useful for diagnostic reagents and therapeutics for condition such as cancer associated with the reference protein (see page 57, lines 1-2, in particular).

Applicants' arguments filed 6/25/07 have been fully considered but are not found persuasive.

Applicants' position is that claim 37 has been amended and the WO98/30582 does not teach antibodies that specifically bind to amino acid residues 105-187.

In response, the WO 98/30582 publication teaches an antibody such as a monoclonal antibody that binds to a protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). The reference antibody made using the reference protein obviously cross-react with the claimed SEQ ID NO: 2.

Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

12. Claims 37-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/30582 publication (of record, July 16, 1998; PTO 892) in view of US Pat No. 6,180,370B (filed June 1995; PTO 892).

The teachings of the WO 98/30582 publication have been discussed supra. The WO 98/30582 publication further teaches the reference antibody is useful for diagnostic reagents and therapeutics for condition such as cancer associated with the reference protein (see page 57, lines 1-2, in particular).

The invention in claim 39 differs from the teachings of the reference only in that the antibody specifically for SEQ ID NO: 2 is a humanized antibody instead of a murine monoclonal antibody.

The '370 patent teaches a method of producing humanized antibodies (See column 44 line 33; column 68 lines 8-44, in particular). The advantages of humanized antibody are that the antibody binds with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce humanized antibody as taught by the '370 patent using the murine monoclonal antibody that binds to EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 or the antibody that binds AAV40509 that is 92.9% identical to the claimed SEQ ID NO: 2 as taught by the WO98/30582 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce humanized antibody because the '370 patent teaches that the advantages of humanized antibody are that the antibody binds with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular). The WO98/30582 publication teaches the reference antibody is useful as a diagnostic reagent and as a therapeutic for conditions associated with the reference protein (see page 57, lines 1-2, in particular).

Applicants' arguments filed 6/25/07 have been fully considered but are not found persuasive.

Applicants' position is that claim 37 has been amended and the WO98/30582 does not teach antibodies that specifically bind to amino acid residues 105-187.

In response, the WO 98/30582 publication teaches an antibody such as a monoclonal antibody that binds to a protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-

33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). The reference antibody made using the reference protein obviously cross-react with the claimed SEQ ID NO: 2.

Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

13. Claims 37-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/30582 publication (of record, July 16, 1998; PTO 892) in view of WO 96/34096 publication (published Oct 1996; PTO 892).

The teachings of the WO 98/30582 publication have been discussed supra. The WO98/30582 publication further teaches the reference antibody is useful for diagnostic reagents and therapeutics for conditions associated with the reference protein (see page 57, lines 1-2, in particular).

The invention in claim 39 differs from the teachings of the reference only in that the antibody specifically for SEQ ID NO: 2 is a human antibody instead of a murine monoclonal antibody.

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim 18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the advantage of the human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to make human antibody that bind to SEQ ID NO: 2 by substituting the antigen EGFR as taught by the WO 96/34096 publication for the antigen EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 or the antibody that binds AAV40509 that is 92.9% identical to the claimed SEQ ID NO: 2 as taught by the WO98/30582 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce human antibody because fully human

antibody is less immunogenic as taught by the WO 96/34096 publication (See page 1, lines 28-35, in particular). The WO98/30582 publication teaches antibody to the reference proteins is useful for diagnostic reagents and therapeutics for conditions associated with the reference protein (see page 57, lines 1-2, in particular).

Applicants' arguments filed 6/25/07 have been fully considered but are not found persuasive.

Applicants' position is that claim 37 has been amended and the WO98/30582 does not teach antibodies that specifically bind to amino acid residues 105-187.

In response, the WO 98/30582 publication teaches an antibody such as a monoclonal antibody that binds to a protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). The reference antibody made using the reference protein obviously cross-react with the claimed SEQ ID NO: 2.

Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

14. Claims 37 and 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/30582 publication (of record, July 16, 1998; PTO 892) in view of US Pat No 6,132,729 (Oct 2000, PTO 892).

The teachings of the WO 98/30582 publication have been discussed supra. The WO98/30582 publication further teaches the reference antibody is useful for diagnostic reagents and therapeutics for conditions such as cancer associated with the reference protein (see page 57, lines 1-2, in particular).

The invention in claim 39 differs from the teachings of the reference only in that the antibody specifically for SEQ ID NO: 2 is a bispecific antibody instead of monospecific monoclonal antibody.

The '729 patent teaches bispecific antibody having the specificity of desired targets for tumor treatment and the bispecific antibody is useful for targeting diverse tumor targets (See column 74, lines 42-52, column 75-76, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce bispecific antibody as taught by the '729 patent using the CDRs from the monoclonal antibody that binds to EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 or the antibody that binds or the antibody that binds AAV40509 that is 92.9% identical to the claimed SEQ ID NO: 2 as taught by the WO 98/30582 publication and other antigen of interest for targeting tumor. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce bispecific antibody because the '729 patent teach that bispecific antibody having the specificity of desired targets for tumor treatment is well known in the art and is useful for against diverse tumor targets (See column 74, lines 42-52, column 75-76, in particular). The WO 98/30582 publication teaches antibody to the reference proteins is useful for as diagnostic reagents and therapeutics for conditions such as cancer associated with the reference protein (see page 57, lines 1-2, in particular).

Applicants' arguments filed 6/25/07 have been fully considered but are not found persuasive.

Applicants' position is that claim 37 has been amended and the WO98/30582 does not teach antibodies that specifically bind to amino acid residues 105-187.

In response, the WO 98/30582 publication teaches an antibody such as a monoclonal antibody that binds to a protein such as EH203_2 (reference SEQ ID NO: 27), which has a long stretch of 166 amino acid residues identical to the claimed SEQ ID NO: 2 (see page 16, line 32-33, page 26, page 35, lines 22-23, page 56, lines 33-34, in particular). The reference antibody made using the reference protein obviously cross-react with the claimed SEQ ID NO: 2.

Since the Patent Office does not have the facilities for examining and comparing the antibody of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best. 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

15. The following new ground of rejection is necessitated by the amendment filed 6/25/07.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 37-39 and 43-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is New Matter.**

The recitation of an isolated antibody or binding fragment thereof specific for the C-terminal region of SEQ ID NO: 2 consisting of amino acid residues **105-187** in claim 37 represents a departure from the specification and the claims as originally filed. The specification does not disclose any antibody or binding fragment that binds to the particular amino acid residues **105-187** of SEQ ID NO: 2. The specification merely discloses antibody AX1A8 and AZ3H6 specifically interact with C-terminal region of MCEMP1, see page 25. However, the specification does not disclose the C-terminal region consisting of amino acid residues 105-187 of SEQ ID NO: 2. The specification discloses the intracellular domain comprising amino acids 1 through 82, a transmembrane domain comprising amino acids 83 through 105 and the extracellular domain comprising amino acids **106 through 187**, see page 6, lines 1-2.

18. No claim is allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

21. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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